DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 12/18/09 are acknowledged.

2. Claims 2-3, 5-6, 9-10, 15-19, 22, 28, 33-36, and 42-50 were cancelled. Claims 1 and 21 were amended.

3. Claims 1, 4, 7-8, 11-14, 20-21, 23-27, 29-32, 37-41, and 51-59 are included in the prosecution.

Response to Arguments

Rejection of claims under 35 USC § 103(a)

4. Applicant's arguments, see Pages 9-14, filed 12/18/09, with respect to the rejection of claims 1, 4, 7, 11-14, 20-21, 23-25, 27, 29-32, 37-41, and 51-59 under 35 U.S.C. 103(a) as being unpatentable over Breitenbach et al. (US 6,150,424) in view of Jane et al. (US 5,710,190) have been fully considered but are not persuasive. Applicant's arguments with respect to the rejection of claims 8 and 26 under 35 U.S.C. 103(a) as being unpatentable over Breitenbach et al. (US 6,150,424) in view of Jane et al. (US 5,710,190) and De Bock et al. (US 5,428,150) have been fully considered but are not persuasive.

Applicant is now using closed language (i.e., "**consisting of**") with respect to the components of the dosage form (line 2 of claim 1 and line 4 of claim 21). Applicant argues that this amendment removes the Examiner's argument that the claims while not affirmatively reciting inclusion of a thermoplastic polymer could include such. Applicant

argues that the Breitenbach et al. patent requires a thermoplastic polymer such as N-vinylpyrrolidone.

This is not persuasive because amended claims 1 and 21, along with the closed "consisting of" language, **also recite optional components** (in part c) such as "a sweetener, a disintegrant, a binder, a lubricant or an opacifier …" Upon further consideration, **a new ground of rejection** is made over Breitenbach et al. (US 6,150,424) in view of Jane et al. (US 5,710,190) and further in view of Amann (US 3,865,935). This new ground of rejection was necessitated by Applicant's amendment since the Amann reference teaches that vinylpyrrolidone is known as a commonly used binder material (Col. 1, lines 52-54). Since the new ground of rejection was necessitated by Applicant's amendment, this action is made FINAL.

Applicant's arguments with respect to the injection molding have been fully considered but are not persuasive because Jane teaches injection molding (Col. 6, lines 24-30) and is combined with Breitenbach. Moreover, instant claims are drawn to a product and the injection molding is a product by process limitation. Applicant is reminded that process limitations cannot impart patentability to a product that is not patentably distinguished over the prior art. In *re Thorpe et al.* (CAFC 1985), supra; In *re Dike* (CCPA 1968) 394 F2d 584, 157 USPQ 581; Tri-Wall Containers, Inc. v. United States et al. (Ct Cls 1969) 408 F2d 748, 161 USPQ 116; In re Brown et al. (CCPA 1972) 450 F2d 531, 173 USPQ 685; Ex parte Edwards et al. (BPAI 1986) 231 USPQ 981.

Claim 59 - Allowable Subject Matter

5. Claim 59 contains allowable subject matter.

6. However, claim 59 also contains trademarks/tradenames. The office action mailed 07/09/08 contained rejections regarding claims with trademarks/tradenames. Although Applicant removed the trademarks/tradenames from claims 11, 12, 29, and 30, the trademarks/tradenames were introduced in claim 59 by amendment (12/22/08). Therefore, a rejection under 35 U.S.C 112, second paragraph follows.

7. An objection to claim 59 (being dependent upon a rejected base claim) also follows.

8. Although claim 59 recites the formulations (examples 1 through 7) in the alternative by using the term “or”, the Examiner suggests that Markush language ("**selected from the group consisting of**") be used in claim 59.

Claim Objections

9. **Claim 59** is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

10. **Claim 59** would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claim 59 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 59 contains the trademarks/trade names Ac-Di-Sol® and MALTRIN®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name Ac-Di-Sol® is used to identify/describe croscarmellose sodium and the trademark/trade name MALTRIN® is used to identify/describe maltodextrin and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1, 4, 7, 11-14, 20-21, 23-25, 27, 29-32, 37-41, and 51-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Breitenbach et al. (US 6,150,424) in view of Jane et al. (US 5,710,190) and further in view of Amann (US 3,865,935).

The claimed invention is a pharmaceutical dosage form suitable for oral administration **consisting of** a molded microcellular polymeric material and a pharmaceutically acceptable active agent. The molded microcellular polymeric material is a non-thermosetting polymerized material comprised of at least one polyol selected from lactitol, xylitol, erythritol, sorbitol, maltitol, or mannitol, or combinations thereof; and at least one of a) non-thermosetting modifier selected from a starch, maltodextrin, a dextrose equivalent, polyalditol, a hydrogenated starch hydrosylate, or a mixture thereof; and/or b) a non-thermosetting polymer selected from carboxymethyl cellulose sodium, methyl cellulose, ethylcellulose, hydroxyethylcellulose (HEC), hydroxypropylmethyl cellulose (HPMC), hydroxypropylmethyl cellulose phthalate, cellulose acetate phthalate, noncrystalline cellulose, starch and its derivatives, and sodium starch glycolate or mixtures thereof; and optionally a sweetener, a disintegrant, a binder, a lubricant or an opacifier; and wherein the molded microcellular polymeric material and pharmaceutically active agent form a single phase homogeneous mixture and are injection molded into the molded microcellular pharmaceutical dosage form.

Breitenbach teaches solid, foamed active ingredient preparations based on melt-processable polymers (Col. 1, lines 5-7). Suitable active ingredients include analgesics (acetylsalicylic acid), antibiotics (amoxicillin), antidepressants (fluoxetine) and antihypertensives (verapamil) (Col. 1, line 38 to Col. 2, line 38). “The active ingredient

preparations may furthermore also comprise starches …" (Col. 3, lines 21-22). Conventional pharmaceutical ancillary substances such as bulking agents (mannitol, sorbitol, xylitol), lubricants (stearates of aluminum or calcium), plasticizers (polyethylene glycol), dyes and stabilizers that can be included in the preparation are also disclosed (Col. 3, lines 26-60). "The degree of foaming of the active ingredient preparation can be controlled by the amount of blowing agent added and the extrusion temperature. A high degree of foaming results in a lower density and thus a high rate of dissolution of the active ingredient form" (Col. 4, lines 61-65). "The foamed active ingredient preparation is subsequently shaped to the required active ingredient forms … by pelleting, granulating or tableting by known processes" (Col. 5, lines 2-5).

Breitenbach does not expressly teach a molded microcellular dosage form wherein the molded microcellular polymeric material and pharmaceutically active agent are injection molded into the pharmaceutical dosage form.

Jane teaches "… a biodegradable, soy protein-based thermoplastic composition. The composition is made of soy protein combined with a foaming agent, an organic plasticizing agent, and an aqueous medium such as water, and additives as desired. Articles formed from the composition have a foamed, cellular structure, and are biodegradable and possess a high degree of tensile strength, low density, and water resistance." (Col. 1, lines 42-51). "The composition is composed of about 100 parts soy protein that is preferably soy protein isolate, … and about 0.1-10 parts of a foaming agent, … about 5-60 parts of an organic plasticizing agent that is preferably glycerol, ethylene glycol or propylene glycol, and about 5-50 parts aqueous medium which is

preferably water. One or more additives such as a filler, lubricant, colorant, preservative, and bleaching/whitening agent, can be included as desired" (Col. 1, lines 54-65). "The mixture can be molded into an article by compression molding" (Col. 2, lines 3-4). "Advantages of the protein based thermoplastics include excellent biodegradability, water resistance, and a low cost production" (Col. 2, lines 11-24). Polyethylene glycol is disclosed as a plasticizer, along with mannitol and maltitol (Col. 3, lines 51-64). Starches including corn or wheat starch can be used as fillers (Col. 4, lines 36-44). "Natural and modified gums such as xanthan gum, guar gum, locust bean gum, gum arabic, alginates, carrageenan, pectin, agar, konjac flour, and the like, can also be included as a filler in the composition" (Col. 4, lines 54-57). Cellulose derivatives such as methylcellulose, carboxymethylcellulose, hydroxymethylcellulose, hydroxypropylcellulose and sodium carboxymethylcellulose can also be used as fillers (Col. 4, lines 58-62). Lubricants and colorants are disclosed (Col. 5, lines 11-35). Examples disclose molded articles with a foamed appearance and a closed cell structure with an average cell diameter of about 50μm (Col. 8, lines 12-14). Injection molding is disclosed (Col. 6, lines 24-30).

Amann teaches that vinylpyrrolidone is known as a commonly used binder material (Col. 1, lines 52-54).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a solid, foamed active ingredient preparation containing starch, polyols (mannitol, sorbitol, xylitol) as taught by Breitenbach, combine it with the foamed microcellular composition and injection molding, as taught by Jane, in view of

the vinylpyrrolidone that is a commonly used binder material, as taught by Amann, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Jane teaches that the foamed microcellular composition has the advantages of excellent biodegradability, water resistance, and a low cost production" (Col. 2, lines 11-24). Since all the claimed elements are found in Breitenbach, Jane, and Amann, one with ordinary skill in the art could have combined the elements and the combination would have yielded predictable results. See *KSR International Co. v. Teleflex Inc.*, 550 U.S. - , 82 USPQ2d 1385 (2007).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 1, the limitation of a pharmaceutical dosage form would have been obvious over the solid, foamed active ingredient preparation that can subsequently be shaped by pelleting, granulating or tableting by known processes, as taught by Breitenbach (Col. 1, lines 5-7 and Col. 5, lines 2-5). The limitation of a molded microcellular polymeric material and a non-thermosetting polymerized plastics material would have been obvious over the starches, mannitol, sorbitol and xylitol as taught by Breitenbach (Col. 2, lines 58-60, Col. 3, lines 21-22 and Col. 3, lines 33-35). The limitation of the molded polymeric material would have been obvious over the molding

of the mixture as taught by Jane (Col. 2, lines 3-4). The limitation of a pharmaceutically acceptable active agent would have been obvious over the active ingredients include analgesics (acetylsalicylic acid), antibiotics (amoxicillin), antidepressants (fluoxetine) and antihypertensives (verapamil), as taught by Breitenbach (Col. 1, line 38 to Col. 2, line 38). The limitation of the non-thermosetting polymerized plastics material that contains at least one polyol and at least one non-thermosetting modifier would have been obvious over the polyols mannitol, sorbitol and xylitol and the starches, as taught by Breitenbach (Col. 3, lines 21-22 and Col. 3, lines 33-35). The limitation of the non-thermosetting polymer would have been obvious over the cellulose derivatives such as methylcellulose, carboxymethylcellulose, hydroxymethylcellulose, hydroxypropylcellulose and sodium carboxymethylcellulose taught by Jane (Col. 4, lines 58-62). The injection molding would have been obvious over the injection molding taught by Jane (Col. 6, lines 24-30). Claim 1 allows the inclusion of optional binder materials and since Amann teaches that vinylpyrrolidone is known as a commonly used binder material (Col. 1, lines 52-54), one of ordinary skill in the art would find it obvious to include binders such as vinylpyrrolidone in the composition with a reasonable expectation of success in producing a functional pharmaceutical composition.

Regarding instant claims 4, 23-24, the limitation of the non-thermosetting polymerized plastics material that contains at least one polyol and at least one non-thermosetting modifier would have been obvious over the polyols mannitol, sorbitol and xylitol and the starches, as taught by Breitenbach (Col. 3, lines 21-22 and Col. 3, lines 33-35).

Regarding instant claims 7 and 25, the limitation of the starch would have been obvious over the starches taught by Breitenbach (Col. 3, lines 21-22) and over the corn starch, wheat starch, rice starch and potato starch taught by Jane (Col. 4, lines 36-44).

Regarding instant claim 27, the limitation of the non-thermosetting polymer that is present in an amount of 2 to 90% w/w would have been obvious over the 5 to 20 parts of filler such as starch, cellulose derivatives such as methylcellulose, carboxymethylcellulose, hydroxymethylcellulose, hydroxypropylcellulose and sodium carboxymethylcellulose taught by Jane (Col. 4, lines 25-62).

Regarding instant claims 11 and 29, the limitation of the disintegrant would have been obvious over the sodium carboxymethylcellulose taught by Jane (Col. 4, lines 58-62) and the guar gum, locust bean gum, and agar as taught by Jane (Col. 4, lines 54-57).

Regarding instant claims 12 and 30, the lubricant would have been obvious over the talc, as taught by Breitenbach (Col. 3, line 53).

Regarding instant claims 13 and 31, the opacifier would have been obvious over the calcium carbonate used as a bleaching/whitening agent, as taught by Jane (Col. 5, lines 5-7).

Regarding instant claims 14 and 32, the pharmaceutically acceptable active agent would have been obvious over the active ingredients include analgesics (acetylsalicylic acid), antibiotics (amoxicillin), antidepressants (fluoxetine) and antihypertensives (verapamil), as taught by Breitenbach (Col. 1, line 38 to Col. 2, line 38).

Regarding instant claims 20 and 37, the limitation of the microcellular polymeric material that results in a closed cell foam would have been obvious over the closed cell structure as taught by Jane (Col. 8, lines 12-14).

Regarding instant claim 21, the limitation of a rigid microcellular foam would have been obvious over the solid, foamed active ingredient preparation as taught by Breitenbach (Col. 1, lines 5-7 and Col. 5, lines 2-5) and by the closed cell structure as taught by Jane (Col. 8, lines 12-14). The limitation of a solid excipient having voids with a maximum void dimension in the range from about 2 to 100 microns would have been obvious over the closed cell structure with an average cell diameter of about 50μm, as taught by Jane (Col. 8, lines 12-14). The limitation of a void fraction in the range of about 5 to 95 percent would have been obvious over the solid foamed active ingredient preparations taught by Breitenbach (Col. 1, lines 5-7) because Breitenbach teaches that "the degree of foaming of the active ingredient preparation can be controlled by the amount of blowing agent added and the extrusion temperature. A high degree of foaming results in a lower density and thus a high rate of dissolution of the active ingredient form" (Col. 4, lines 61-65). One with ordinary skill in the art would modify the process parameters by varying the amount of blowing agent and the extrusion temperature and achieve the desired void fraction. The recited void fraction range would have been an obvious variant unless there is evidence of criticality or unexpected results. The limitation of the solid excipient comprising a thermosetting polymerized plastic material and an active pharmaceutical agent combined in a homogenous solid mixture would have been obvious over the solid foamed active ingredient preparations

taught by Breitenbach (Col. 1, lines 5-7). The limitation of optionally comprising a sweetener, a disintegrant, a binder, a lubricant or an opacifier would have been obvious over the lubricants (stearates of aluminum or calcium) taught by Breitenbach (Col. 3, lines 26-60) and the additives such as lubricants and colorants as taught by Jane (Col. 5, lines 11-35). Claim 21 allows the inclusion of optional binder materials and since Amann teaches that vinylpyrrolidone is known as a commonly used binder material (Col. 1, lines 52-54), one of ordinary skill in the art would find it obvious to include binders such as vinylpyrrolidone in the composition with a reasonable expectation of success in producing a functional pharmaceutical composition.

Regarding instant claim 38, the limitation of the homogenous solid mixture that has a sufficiently high solubility in saliva would have been obvious over the “solid, foamed active ingredient preparations ... which comprise the active ingredient homogenously dispersed in the polymeric matrix, dissolve very rapidly and thus permit rapid release of the active ingredient”, as taught by Breitenbach (Col. 6, lines 18-22).

Regarding instant claim 39, the voids that are in the form of closed cells would have been obvious over the closed cell structure taught by Jane (Col. 8, lines 12-14).

Regarding instant claim 40, the limitation of the rigid microcellular foam that is enclosed within a skin would have been obvious over the “closed active ingredient forms, i.e., forms in which the layer comprising active ingredient is completely enveloped by a layer without active ingredient” as taught by Breitenbach (Col. 5, lines 9-60). Breitenbach teaches the "production of multilayer partially or completely foamed forms comprising active ingredients by coextrusion. This entails at least two

compositions ... at least one of which comprises an active ingredient and at least one of which is impregnated …" (Col. 5, lines 9-15). One with ordinary skill in the art would find it obvious to completely impregnate the active ingredient layer with another active ingredient layer during the process of routine experimentation.

Regarding instant claim 41, the limitation of the overall density of the dosage form that is substantially less than that of stomach fluids, whereby the dosage form is gastro-retentive would have been obvious because Breitenbach teaches that "the degree of foaming of the active ingredient preparation can be controlled by the amount of blowing agent added and the extrusion temperature. A high degree of foaming results in a lower density and thus a high rate of dissolution of the active ingredient form" (Col. 4, lines 61-65). One with ordinary skill in the art would modify the density of the dosage form with respect to the density of stomach fluids during the process of routine experimentation in order to make the dosage form gastro-retentive.

Regarding instant claim 51, the limitation of the non-thermosetting modifier that is present in an amount of 5 to 50% w/w would have been obvious over the 5 to 20 parts of filler such as starch taught by Jane (Col. 4, lines 25-44).

Regarding instant claims 52-54 and 57-58, the limitation of the polyol that is present in an amount of 5 to 70% w/w, in an amount of 5 to 50% w/w, and in an amount of 5 to 25% w/w would have been obvious over the 5 to 60 parts of plasticizer such as mannitol, and maltitol taught by Jane (Col. 3, lines 44-64).

Regarding instant claims 55-56, the limitation of the non-thermosetting modifier that is present in an amount of 2 to 90% w/w, and in an amount of 5 to 50% w/w would

have been obvious over the 5 to 20 parts of filler such as starch taught by Jane (Col. 4, lines 25-44). The recited range of the non-thermosetting modifier would have been an obvious variant unless there is evidence of criticality or unexpected results.

15. Claims 8 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Breitenbach et al. (US 6,150,424) in view of Jane et al. (US 5,710,190), Amann (US 3,865,935) and De Bock et al. (US 5,428,150).

The teachings of Breitenbach and Jane are stated above.

Breitenbach and Jane do not expressly teach a maltodextrin as a non-thermosetting modifier.

De Bock teaches “a process for the extrusion of a starch-containing composition to produce a material suitable for the production of moulded articles in which the composition contains in addition to the starch a starch degradation product selected from starch hydrolysis products having DE's of 1 to 40, particularly a maltodextrin …” (Abstract). “The hydrolysis products used in the process … are preferably maltodextrins and more preferably have DE values of 2 to 20” (Col. 3, lines 50-52).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a solid, foamed active ingredient preparation, as taught by Breitenbach, combine it with the foamed microcellular composition, as taught by Jane, further combine it with the maltodextrins, as taught by De Bock, and produce the instant invention.

One of ordinary skill in the art would do this because De Bock teaches that maltodextrins are degradation products of starch and the lower the DE value of the maltodextrin the less the extent of starch degradation (Col. 3, lines 36-47). One with ordinary skill in the art would find it obvious to try maltodextrin in the solid, foamed active ingredient preparation and the starches taught by Breitenbach (Col. 3, lines 21-22) and in the foamed microcellular composition with the corn starch, wheat starch, rice starch and potato starch taught by Jane (Col. 4, lines 36-44) with a reasonable expectation of success of producing a functional molded microcellular polymeric dosage form.

Regarding instant claims 8 and 26, the limitation of the non-thermosetting modifier that is a maltodextrin would have been obvious over the maltodextrins and starches taught by De Bock (Abstract and Col. 3, lines 50-52) and over the starches taught by Breitenbach (Col. 3, lines 21-22) and Jane (Col. 4, lines 36-44).

Conclusion

16. Claim 59 contains allowable subject matter.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached at 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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